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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/582,486	11/16/2000	Christopher Joseph Schofield	P02005US0	3471

26271 7590 10/20/2004

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EXAMINER

BORIN, MICHAEL L

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/582,486

Applicant(s)

SCHOFIELD ET AL.

Examiner

Michael Borin

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 07/23/2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 12,37,39,40,52,55,57,58,233 and 234 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 12,37,39,40,52,55,57,58,233,234 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____.

DETAILED ACTION

Status of claims

1. Amendment filed 07/23/2004 is acknowledged. Claims 233,234 are added. Claims 12,37,39,40,52,55,57,58,233,234 are pending. All other claims are canceled.

It is noted that identifier of claim 37 is incorrect. The claim is "currently amended", not "previously added".

Also, it is noted that claims 37 and 40, as amended, are identical duplicates. Consequently, claims 55,58 are identical duplicates also.

Further, claim 39 is amended to include subject matter which was subject of restriction in the previous Office action (see Group V) – it incorporated residues recited in now canceled claim 13. Applicant is requested to amend the claim to delete the non-elected subject matter.

The claims are addressed to the extent they read on the elected species - DAOCS with modification of Leu158 residue.

2. Rejections not reiterated from previous Office actions are hereby withdrawn. The following rejections and objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Rejections under 35 U.S.C. § 102 are withdrawn in view of amendment of the claims to remove claim language "having significant sequence similarity".

Claim objections

3. Claims 52,55,57,58 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim Rejections - 35 USC § 112, second paragraph.

4. Claims 12,37,39,40,52,55,57,58,233,234 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The claims are now limited to "a DAOCS enzyme" having replacements at residues recited in claim 12, and specification is amended to identify the DAOCS being crystallized as SEQ ID No. 1. The residues recited in claim 12 are residues of a particular protein., DAOCS from *S. clavuligerus* of SEQ ID No. 1 There is no indication that any other "DAOCS enzyme " has exact same residues. Hence the claims are not clear as to which residues are to be replaced in enzymes other than protein SEQ ID No 1. Same for claims 37, 40 also reciting particular residues of SEQ ID No. 1.

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B. (corresponds to 10B in previous Office action) Further applicant argues that now it is clear what is being modified as the claims are now limited to "a DAOCS enzyme". Examiner maintains that as it is not clear what is being modified because neither binding site nor any other residues have been identified to any DAOCS other than DAOCS from *S. clavuligerus* of SEQ ID No. 1 .

Applicant points at Fig. 2 as sufficient to describe penicillin binding site. However, said Figure, first, reflects binding site for penicillin nucleus, not binding site for penicillin side chain. Second, all Fig 2 demonstrates is residues of particular enzyme of SEQ ID No. 1, and does not identify residues participating in binding in other enzymes.

C. (corresponds to 10D in previous Office action). Examiner maintains that it is not possible to define metes and bounds for mutations claimed in claims 52,55, 57,58 because it is not clear what is the scope of "interactions" is addressed. The representative examples recited at the end of the claims do not define the scope of "binding interactions".

Applicant argues that structure provided in application shows amino acids that are close enough to each other to be capable of binding interaction". It is not clear what proximity has to do with the nature of "binding interactions" addressed in the claim. Further, as addressed above, specification demonstrates residues of particular enzyme of SEQ ID No. 1, and does not identify residues participating in binding in other enzymes.

Claim Rejections - 35 USC § 112, first paragraph (enablement).

5. In regard to claims 12,37,39,40, in view of amendment limiting scope of the claims the enablement rejection is changed to scope of enablement rejection:

Claims 12,37,39,40,52,55,57,58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the particular DAOCS of SEQ ID No. 1, does not reasonably provide enablement for any other DAOCS. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The only structure of a DAOCS enzyme demonstrated in specification is the structure of DAOCS from *S. clavuligerus* of SEQ ID No. 1. There is no indication that any other "DAOCS enzyme" has exact same residues. Neither binding site nor any other residues have been identified to any DAOCS other than DAOCS from *S. clavuligerus* of SEQ ID No. 1. There is no guidance on how to identify binding site and/or particular residues in other DAOCS enzymes. Figure 2, addressed by applicant, reflects binding site for penicillin nucleus, not binding site for penicillin side chain and does not guide on how to identify binding site and/or particular residues in other DAOCS enzymes. Hence the claims are not clear as to which

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residues are to be replaced, inserted or deleted in enzymes other than protein SEQ ID No 1.

6. In regard to claims 52,55,57,58,233,234 the enablement rejection addressing the issue of further mutations is maintained for the reasons of record and in view of the following:

The claims are drawn to enzymes further modified by "two or more mutations" that "create or delete a binding interaction". Neither full scope of interactions, nor amount of mutations (the claim language is open ended and encompasses unlimited number of mutations) is clearly identified in the specification. Applicant argues [in response to 11(4)] that the DAOCS structure provided by applicant is sufficient to allow prediction of mutation that could create or delete a binding interaction. Examiner disagrees. In regard to "creating" binding sites, there is no guidance on how and where to create these binding sites and how such modification in structure will result on biological activity of the product. Accordingly, an artisan would not know how to make the product as claimed. In regard to "deleting" interactions, even though there is some identification of the role of particular residues (note, however, that this information is limited to of DAOCS from *S. clavuligerus* of SEQ ID No. 1), there is no guidance on what can be deleted by "two or more mutations" that would not impair the intended DAOCS biological activity.

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In view of the above, it is the Examiners position that with the insufficient guidance and working examples and in view of unpredictability and the state of art one skilled in the art could not make and/or use the invention with the claimed breadth without an undue amount of experimentation.

Response to arguments

Applicant argues that the demonstration of structure of DAOCS allows further modification. Examiner agrees that it does enable modification of known structure of DAOCS from *S. clavuligerus* of SEQ ID No. 1. But it does not enable modification of other DAOCS enzymes. Nor it enables addition or deletion of other binding sites by way of introducing indefinite amount of mutations.

Further, applicant provides examples of successful replacement of Leu 158. Once again, Examiner does not question that this particular residue in this particular molecule can be replaced, but rather questions further mutations and/or application to other DAOCS enzymes.

With respect to further publications of other researchers, the enablement sufficiency of a specification is determined as of filing date. *Hybritech, Inc. V. Monoclonal antibodies, Inc.*, 231 USPQ 81 (Fed. Cir. 1986)

Claim Rejections - 35 USC § 112, first paragraph (written description, new matter).

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7. Claims 30, 37 9and claims dependen thereupon) are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Claims 30, 34, 38 introduce new matter as they use the phrase "deletion" in regard to residues within the region 300-311. There is no disclosure in the specification of such modification of enzyme's structure.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will

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the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. Dr. Borin can normally be reached between the hours of 8:30 A.M. to 5:00 P.M. EST Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Michael Woodward, can be reached on (571) 272-0722.

Any inquiry of a general nature or relating the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0549.

MICHAEL BORIN, PH.D
PRIMARY EXAMINER

10/15/04

mlb

